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TITLE: Imaging Prostate Cancer Microenvironment by Collagen Hybridization

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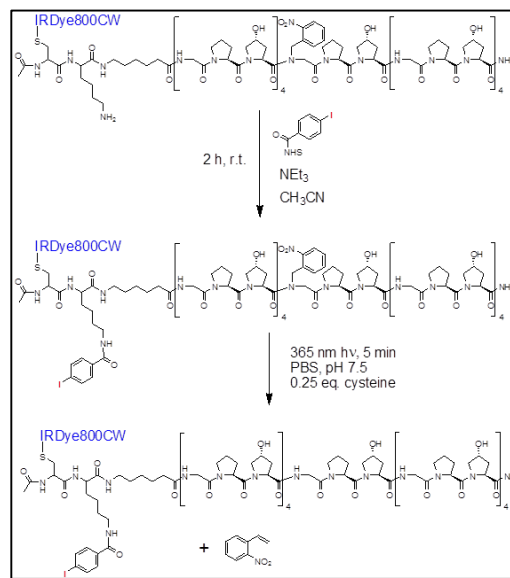
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INTRODUCTION: Small collagen mimetic peptide (CMPs) that mimic the amino acid sequence and three dimensional structure of collagen were shown to have specific binding affinity to type I collagen fibers. Although the exact mechanism of binding is not known fully, evidence is accumulating that supports the idea that the CMP is binding to partially denatured domains of natural collagen by triple helical hybridization. Here we use CMP as a collagen targeting agent that will allow imaging of prostate cancer (PCa). Since CMP binds to unstructured collagen domains more readily, it is expected to exhibit selective affinity to metastatic PCa known to contain processed and denatured collagens. This is the first time that the remodeled ECM of tumor microenvironment is targeted for cancer imaging which is an entirely new way to image PCa with a potential to revolutionize the cancer community with respect to imaging and possibly treating PCa and its microenvironment.

1. **KEYWORDS:** molecular imaging; near-infrared imaging; SPECT; collagen mimetic peptide; prostate cancer; tumor microenvironment
2. **ACCOMPLISHMENTS:**
 - **What were the major goals of the project?**
 - (1) Dual radio- and fluorescent labeling of CMPs retaining high-affinity and specificity for intact and digested collagen (type I) films; (2) Validation of dual-labeled CMPs that display high affinity and specificity for stromal collagens in frozen PCa xenografts; and, (3) Measurement of pharmacokinetics and *in vivo* imaging of dual-labeled CMPs in mouse subcutaneous PC-3 xenograft (and pancreatic xenograft) models.
 - **What was accomplished under these goals?**

In year three, we focused on two dual-labeled CMP analog that allow for gentle radiolabeling conditions and we tested it *in vivo* for its pharmacokinetic profile in a transgenic and subcutaneous model of PCa. We first tried a follow up SPECT-CT imaging experiment using a dual labeled CMP with [¹²⁵I]SIB and IRDye800CW in a transgenic F1 FVB/TRAMP mouse with severely hypertrophied seminal vesicles. The radiolabeling of this analog is shown in Scheme 1. In healthy mice, this analog rapidly washed out (progress report, year 2). In mice with enlarging, diseased seminal vesicles, this dual labeled CMP bound to the enlarged vesicles and little else as seen by NIRF imaging (Fig. 1A, red). CMP binding overlapped with an inflammation probe that was co-injected (DPA-713-IRDye680LT, green), suggesting the CMP was binding to inflammation-induced tissue remodeling. SPECT-CT imaging of the same animal on the same days as NIRF imaging revealed rapid washout of the CMP from everything except tissue in the lower right quadrant. The SPECT signal remains the same through 24 and 48 hours post-injection, suggesting stable radiotracer accumulation although the SPECT



Scheme 1. Conjugation of [¹²⁵I]SIB to Ac-C(IRDye800CW)-K-CMP₉-CONH₂ and photo decaying.

signal does not match the observed fluorescence signal in both inflamed seminal vesicles. This particular analog did not produce matching NIRF and SPECT signal distributions in this model. This supports earlier results showing *in vivo* lability of the radioiodine label despite using the *p*-iodobenzoyl group and the adjacent bulky dye.

In an effort to move away from radioiodine and what appears to be *in vivo* dehalogenase activity, we next synthesized and radiolabeled a dual labeled CMP instilled with both IRDye800CW and CHX-A-DTPA, which chelates In-111 under gentle conditions. Scheme 2 depicts the structure and labeling conditions. We then tested this analog in a subcutaneous model of PCa in which mice (n = 4) bore one each of a PC-3 PIP tumor with generally higher collagen remodeling and one PC-3 flu tumor with less. Figure 2 shows the SPECT-CT images of CMP distribution in the first 6 hours after injection. One mouse was injected with still-caged (inactive) CMP while the remaining four mice were injected with UV-activated labeled CMP. Scant tumor accumulation was observed in the mice until 6 hours after injection. At that time, the PC-3 PIP tumor retained radiotracer signal at the edges of the tumor while the PC-3 flu tumor displayed very little (3D projection and inset). The mouse injected with still-caged CMP displayed very little tumor uptake although had some uptake in the neck. All mice displayed high radiotracer uptake in the liver and kidneys, as it also appears using NIRF detection (data not shown).

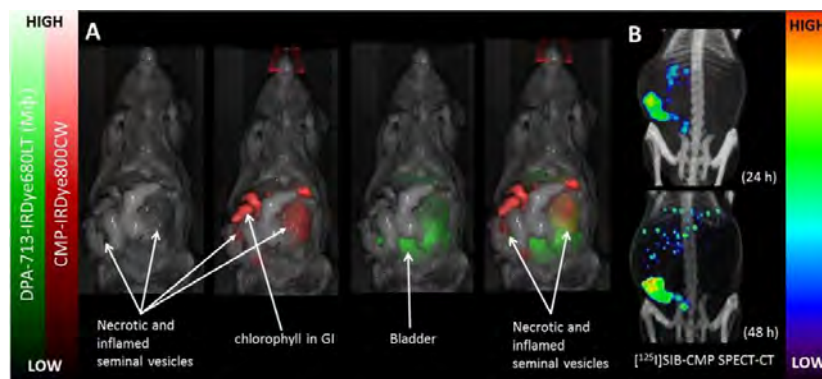
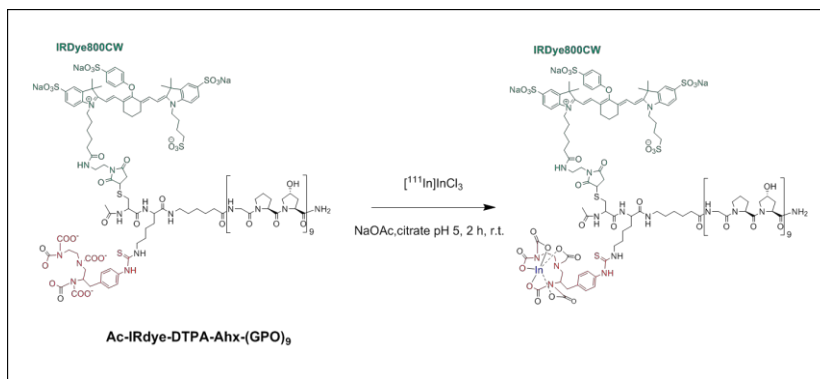


Figure 1. NIRF and SPECT-CT imaging in an F1 TRAMP mouse. A male TRAMP mouse devoid of prostate cancer but containing hypertrophied, inflamed seminal vesicles was scanned using CMP-800CW and an inflammation tracer, DPA-713-IRDye680LT using NIRF imaging. Both inflamed seminal vesicles are displaying CMP uptake (red) co-localizing with the inflammation marker in green. SPECT-CT imaging of the same animal with [^{125}I]SIB- CMP shows intense radiotracer uptake at both 24 and 48 h post-injection in the lower right quadrant, possibly representing GI clearance.



Scheme 2. Radiolabeling of [^{111}In](lys₂)CHX-A-DTPA-(cys₁)IRDye800CW-CMP₉.

At 24 h post-radiotracer injection, higher tumor uptake was apparent in all of the mice except the mouse injected with still-caged (inactive) CMP (Fig. 3). CMP distribution within the tumors was enriched at the edges where growth is occurring. By 24 h, PC-3 flu tumors were also taking up labeled CMP, except in one mouse. Liver and renal uptake of CMP persisted, even in the still-caged CMP mouse, indicating non-specific metabolic excretion in these tissues. This is undesirable and will prompt the pursuit of dye-free CMP analogs as the dye is targeting this excretion pathway.

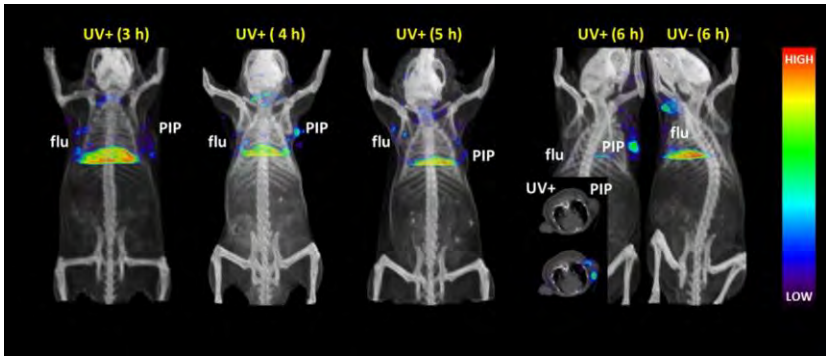


Figure 2. [^{111}In](CXH-A)-(lys₂)-DTPA-CMP₉-(cys₁)-IRDye800CW SPECT-CT at 3-6 h post-injection. Five mice, each bearing a single PC-3 PIP (higher Δ collagen) and PC-3 flu (lower Δ collagen) tumor xenograft, were injected with radiolabeled CMP and imaged by SPECT-CT at the indicated times. PIP tumor uptake of CMP was favored in most mice with the 6 h time point showing clear accumulation of de-caged CMP while still-caged CMP displayed almost no uptake. Liver and renal uptake dominated however (not shown), making tumor uptake appear relatively weak.

We finished probing the library of PCa xenografts to reflect androgen receptor sensitivity status, expression of the biomarker PSMA and speed at which the tumors were growing. Mice bearing an LAPC4 (AR⁺, androgen sensitive, PSMA moderate, moderately rapid growth rate) or a C4-2 (AR^{mut}, androgen insensitive, PSMA low, slow growth rate of primary with fast growth rate of local secondary) were injected with a fluorescent-only CMP-IRDye800CW analog followed by MMPSense680 (Perkin Elmer) and the tumors were harvested 72 h (CMP), 24 h (MMPSense) later. Frozen sections of 20 μm thickness were made and scanned using a LI-COR Odyssey scanner. The scans revealed very low CMP uptake in the slow growing primary C4-2 tumor while the fast growing local secondary offshoots displayed CMP binding throughout (Fig. 4, *in vivo* inset and section). MMPSense680 probe showed high MMPase activity in the secondary offshoots but not in the large primary tumor, providing rationale for extracellular matrix remodeling in the secondary tumors where CMP binding is observed.

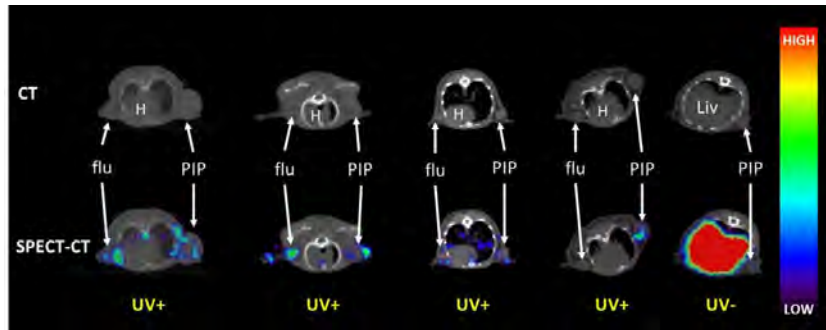


Figure 3. [^{111}In](CXH-A)-(lys₂)-DTPA-CMP₉-(cys₁)-IRDye800CW SPECT-CT at 24 h post-injection. By 24 h post-injection, the same mice in figure 3 displayed stronger CMP uptake at the edges of the tumors, where the tumors are expanding. At this time point, both PC-3 PIP and PC-3 flu tumors are taking up the CMP probe except in the mouse receiving still-caged CMP. "H" represents heart and "Liv" represents liver.

LAPC4 xenografts display a moderately rapid rate of growth and were found to contain a somewhat lower amount of CMP uptake compared with the fast-growing C4-2 secondary tumors. MMPSense uptake was lower than in the secondary C4-2 growths and took on a focal branching pattern, which is also seen in the CMP distribution (green inset). Overall, these uptake patterns in LAPC4 and C4-2 are consistent with the patterns observed for tumor growth rate in the rest of the xenograft library reported in the last progress update.

Conclusions this period.

Chemistry conditions for the conjugation or radiometallation of IRDy-labelled CMPs appear to greatly affect the integrity of the dye and/or the nitrobenzoyl photo cage group.

Deviations away from pH 6-8 and heating are to be avoided. Our current strategy of using CHX-A-DTPA for subsequent aqueous radiometallation with In-111 is likely to afford an intact labeled CMP that is also biologically stable. Our studies with subcutaneous xenografts are very encouraging with liver and kidney binding now to be avoided.

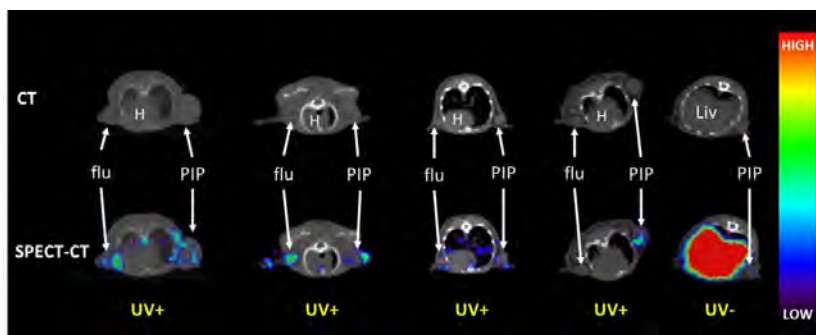


Figure 4. CMP and MMPsense activity in C4-2 and LAPC4 xenografts. Athymic nude mice bearing either a slow growing C4-2 xenograft with fast-growing secondary growth or a fast-growing LAPC4 xenograft were injected with 4 nmol of CMP-IRDye800CW and a single dose of MMPsense680. The mice were sacrificed and imaged at 72 h post-CMP and 24 h post-MMPsense. The tumors were then collected, sectioned and imaged to reveal the pattern of CMP distribution relative to MMP activity. Fast-growing tumor tissue took up and retained CMP probe while slow-growing primary C4-2 tissue took up very little. MMPase activity was prevalent in the fast growing C4-2 nodule as well as the LAPC4 but not the primary C4-2 tissue.

Experiments using CMP₉-IRDye800CW to map collagen remodeling signatures within mice bearing a range of selected subcutaneous prostate cancer xenografts resulted in the observation of a trend in which CMP-800 accumulates with higher density in rapidly growing tumors. This trend was also observed in similarly prepared mice bearing subcutaneous xenografts of pancreatic cancer origin. We have finished the probing of our existing prostate cancer library and have confirmed the trend of CMP binding to growth kinetics to be conserved.

The concurrent binding of MMPsense™, reporting on the enzymatic activities of MMPs 2, 3, 9 and 13, to each of the tumor models described above revealed no trend in discerning tumor growth kinetics, propensity to metastasize and equally bound to tumor xenografts and benign inflamed lymph nodes while CMP-800 bound to tumors but not benign inflamed lymph nodes.

- **What opportunities for training and professional development has the project provided?**
 - Not intended for professional development.

- **How were the results disseminated to communities of interest?**
 - Nothing to report at the present time.
 - **What do you plan to do during the next reporting period to accomplish the goals?**
 - During the next period we intend to optimize the radiolabeling procedures further and analyze the results from the corresponding images.
3. **IMPACT:**
- **What was the impact on the development of the principal discipline(s) of the project?**
 - We have achieved a biologically stable dual-modality CMP but it suffers from high liver and kidney uptake. We have determined that CMP binding does clearly distinguish between tumor and benign enlarged lymph nodes in our mouse model library of xenograft lines. Additionally, CMP uptake appears to distinguish between rapidly growing and slowly growing xenografts while MMPsense probe does not.
 - **What was the impact on other disciplines?**
 - Nothing to report at this time as we have not yet published.
 - **What was the impact on technology transfer?**
 - Nothing to report at this time.
 - **What was the impact on society beyond science and technology?**
 - Nothing to report at this time.
4. **CHANGES/PROBLEMS:** Nothing to report
5. **PRODUCTS:** Nothing to report – These items will be reported once finished with the project and publications are submitted.
6. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**
- **What individuals have worked on the project?**
 - No change
 - **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
 - Martin Pomper

Ended

Title: PSMA-Based Cancer Imaging Agents

Time Commitments: 0.24 calendar months

Supporting Agency: NCI, R01CA134675 (NCE)

Grants Contact: Barbara Croft (301) 496-9531 E-Mail: croftb@mail.nih.gov

PI: Martin Pomper

Performance Period: 4/1/2009-2/28/2015

Level of Funding: \$159,199

Description of Goals: Prostate cancer (PCa) is the leading cancer in the U.S. population and the second leading cause of cancer death in men (16). Therapy for locally advanced disease remains contentious and an increasing number of disparate options are available. Perhaps the most pressing issue in PCa management is the need to predict, at the time of diagnosis, which tumors will remain indolent and which will progress rapidly. The ability to fulfill that goal would eliminate the prostate-specific antigen (PSA)-mediated over detection and overtreatment of clinically insignificant disease.

Aim #1: Synthesis and evaluation of a series of PET imaging agents for PSMA.
Aim #2: Synthetic optimization of the best compounds of Aim 1 en route to GMP and/or facilitated use.
Aim #3: Synthesis and evaluation of a series of homo- and heterodimeric imaging agents for PSMA.

Title: BETR Therapy of Herpesvirus-associated Tumors
Time Commitments: 1.09 calendar months
Supporting Agency: NCI, NIH R01CA138636
Grants Contact: Jason Gill (301) 496-7240 E-Mail: gilljas@mail.nih.gov
PI: Martin Pomper
Performance Period: 04/01/10-02/28/15
Level of Funding: \$322,099
Description of Goals: The purpose is to treat gammaherpesvirus-associated tumors with [131]FIAU in human subjects
Aim #1: To perform a first-in-man, FIAU-PET image-guided, BETR study in patients with EBV-associated malignancies.
Aim #2: To assess parameters that will aid in the optimization of therapy.

Title: TK-based Infection Imaging
Time Commitments: 0.24 calendar months
Supporting Agency: NIH, NIBIB R01EB009367 (NCE)
Grants Contact: Florence Turska (301) 496-9314 E-Mail: ft7p@nih.gov
PI: Martin Pomper
Performance Period: 05/15/10-04/30/15
Level of Funding: \$267,740
Description of Goals: The goal is to study further musculoskeletal infection, comparing a newly developed method in infection imaging to the current clinical standard of tagged white blood cell (WBC) and attempting to determine the sensitivity and specificity of our technique.
Aim #1: Estimate the sensitivity and specificity of FIAU-PET in detecting orthopedic infection.
Aim #2: To extend the FIAU imaging technique to pulmonary infection.
Aim #3: To transition from [124I]FIAU to [18F]FIAU for imaging bacterial infection.

Title: Precision Measurement in Rheumatoid Arthritis
Time commitments: 0.09 calendar months
Supporting Agency: Sibley Hospital 90048894 (NCE)
Grants Contact: Robert L. Sloan, President and CEO; 5255 Loughboro Rd, N.W., Washington DC 20016; 202-537-4680
PI: Rosen
Role: Co-Investigator
Performance Period: 11/1/2011-10/31/2014
Level of Funding: \$600,035
Description of Goals: The long term goal of this aim is to improve the utility of MR imaging in evaluation of RA

Aim 1: A graded approach, extending from basic studies to those with an obvious pathway to clinical translation by providing the following specific aims, which focus on molecular imaging.

Aim 2: A graded approach, extending from basic studies to those with an obvious pathway to clinical translation by providing the following specific aims, which focus on high-field magnetic resonance (MR) (Aim 2) imaging.

Title: Molecular Imaging for Macrophage-Associated Pulmonary Inflammation

Time commitments: 0.36 calendar months

Supporting Agency: NIH/NHLBI 1R01HL116316

Grants Contact: Kimberly Stanton, (301) 435-0519, E-Mail stantonk@nhlbi.nih.gov

PI: Sanjay Jain

Performance Period 9/25/2012- 6/30/2015

Level of Funding: \$238,000

Role: Co-Investigator

Description of Goals: The overall goal is to have a fully validated probe ready for human administration and to file a FDA Investigational New Drug (IND) application at the end of the funding period.

Aim 1: To evaluate [125/4I]DPA-713-SPECT/ PET as a biomarker for serial monitoring of macrophage-associated pulmonary inflammation.

Aim 2: To perform cGMP synthesis and toxicology studies for iodo-DPA-713.

Aim 3: To quantify and correlate lesion-specific, multi-modality image parameters across different time-points using in-house computer-assisted image analysis tools.

Title: Extrathalamic nAChR-PET for Imaging Neurodegeneration

Time Commitments: 0.46 calendar months

Supporting Agency: NIHR33AG037298

Grants Contact: Jessica Perez, 301-496-1472, E-Mail: perezj@nia.nih.gov

PI: Andrew Horti

Role: Co-Investigator

Performance Period: 03/1/2011-8/31/2015

Level of Funding: \$249,274

Description of Goals: The goal is to develop a new nicotinic receptor-based PET agent that enables imaging of extrathalamic sites.

Aim 1, R21. To develop a method of synthesis of sufficient quantities (100-300 mg) of precursor (-)JHU87571 for radiolabeling of [18F]XTRA for 100 radiosyntheses.

Aim 2, R21. To evaluate [18F]XTRA in mice. (a) To confirm that in vivo [18F]XTRA binds at nAChR selectively and specifically. (b) To show that the radioactive metabolites are not present in the mouse brain. (c) To carry out radiation dosimetry studies in mice for an eIND application.

Aim 3, R21. To characterize [18F]XTRA in baboon PET studies. (a) To confirm that the high nAChR binding potentials in cortex, hippocampus and putamen ($BP \geq 1.1$) and optimally rapid brain kinetics were not unique to the single experiment of the Preliminary studies.

Title: Multi-Color Exchange Transfer Imaging of Drug Delivery Nanocarriers

Time Commitments: 0.09 calendar months

Supporting Agency: NIH R01EB01531

Grants Contact: Guoying Liu, 301-594-5220, E-Mail: liug@mail.nih.gov

PI: Michael McMahon

Role: Co-Investigator

Performance Period: 8/1/2011-6/30/2015

Level of Funding: \$439,205

Description of Goals: This proposal is focused on the production of carriers for cervical tumor drugs which are labeled with DIACEST contrast agents for MRI monitoring.

Aim #1: To design a library of peptide-based DIACEST contrast agents suitable for incorporation into biodegradable particles

Aim #2: To design CEST drug carriers optimized for systemic nanoparticle-based chemotherapy

Aim #3: (A) To design CEST drug carriers optimized for local nanoparticle-based chemotherapy. (B) To test imaging after local and systemic administration.

New

Title: PSMA Directed Imaging of Prostate Cancer Focus on Androgen Receptor Dynamics

Time Commitments: 1.35

Supporting Agency: NIH/NCI U01CA183031

Grants Contacts: Yantian Zhang; Program Official; 240-276-5980; Yantian.zhang@nih.gov

PIs: Pomper/Deweese

Performance Period: 11/01/2014-10/31/2016

Level of Funding: \$496,642

Description of Goals: The overall goal is to validate at least two positron-emitting, PSMA-targeted imaging agents clinically so that they can be used to full advantage in supporting existing and emerging therapies for a spectrum of patients suffering from PCa.

Aim 1. To image treatment-naïve patients with localized-locally advanced primary PCa using DCFBC-PET/magnetic resonance imaging, and correlate signal with that on MR concurrently obtained, as well as with tumor grade, PSMA expression and androgen receptor (AR) signaling before and after two months of neoadjuvant androgen deprivation (ADT).

Aim 2. To image patients with CRPC using DCFBC-PET/MR and correlate findings with bone and soft tissue biopsy.

Aim 3. To image patients with CRPC with DCFBC-PET/MR and correlate with standard ^{99m}Tc-based bone scan to guide stereotactic body radiation treatment (SBRT) in patients with oligometastatic disease.

Aim 4. Imaging CRPC with the second-generation, PSMA-targeted PET agent, [18F]DCFPyL.

Title: High-Specificity Imaging Agents for Aggressive Prostate Cancer

Time commitments: 1.35 calendar months

Supporting Agency: NIH/NCI (Renewal) R01CA134675

Grants Contact: Leota Hall; Program Official; 240-276-6449; halle@gmail.nih.gov

PI: Pomper

Performance Period: 12/1/2014-11/30/2019

Level of Funding: \$443,885

Description of Goals: The goals of this project are to leverage existing but untested agents and to develop new agents for imaging PC, with a focus on aggressive, localized disease.

Aim 1: Imaging of patients with biopsy-proved primary PC with DCFPyL-PET with subsequent correlation of PET signal with histopathology at prostatectomy for PSMA expression, Gleason score and other markers

Aim 2: Synthesis of select PSMA-targeted imaging agents that (a) encompass a new scaffold to engender superior affinity and pharmacokinetics; (b) are hetero-bivalent (HtBv), homing to a rationally chosen co-target (in addition to PSMA); or, (3) enable detection with MR through signal amplification

Aim 3: Development and testing of new agents for imaging the PC microenvironment

Title: Direct Test for Neuroinflammation with [11C]DPA-713-PET Scanning

Time commitments: 1.20 calendar months

Supporting Agency: DoD W81XWH-14-1-0620

Grants Contact: Kathy Robinson, GWIRP Grants Officer; 820 Chandler St, Fort Detrick MD 21702

PI: Pomper

Period of Performance: 07/01/2014-06/30/2019

Level of Funding: \$389,978

Description of Goals: This project concerns measuring two key neurological aspects of Gulf War Illness (GWI), namely, neuroinflammation and dysregulation of muscarinic cholinergic transmission.

Aim 1. To assess the degree of microglial activation in the brains of former Gulf War veterans who suffer from GWI through [11C]DPA-713 PET.

Title: Bipolar Androgen Therapy: Breaking out of the Chrysalis of Chronic Androgen Deprivation Therapy in Men with Late-Stage Castrate Resistant Prostate Cancer

Time commitments: 0.12 calendar months

Supporting Agency: CDMRP

Grants Contact: TBD

PI: Denmeade

Co-Investigator: Pomper

Performance Period: 09/1/2014-08/31/2017

Level of Funding: \$1,669,328

Aim 1: The major objective is to demonstrate the superiority of BAT vs. Enza in asymptomatic men with metastatic CRPC progressing after ADT and Abi, by performing a multi-institutional, open-label, randomized study, using radiographic progression-free survival (rPFS) as the primary endpoint.

Aim 2: Evaluate the effect of BAT on the uptake of FDHT and PSMA inhibitor-based PET agents in metastatic sites.

Aim 3: Evaluate regulation of AR splice variants in circulating tumor cells (CTCs) in response to therapy.

Aim 4. Analyze circulating tumor DNA to determine the effect of individual therapies on emergence of AR mutations.

- Catherine Foss

Ended:

Title: Precision Measurement in Rheumatoid Arthritis

Time commitments: 1.20

Supporting Agency: Sibley Hospital 90048894 (NCE)

PI: Rosen

Role: Co-Investigator

Performance Period: 11/1/2011-10/31/2015

Level of Funding: \$600,035

Description of Goals: The long term goal of this aim is to improve the utility of MR imaging in evaluation of RA

Aim 1: A graded approach, extending from basic studies to those with an obvious pathway to clinical translation by providing the following specific aims, which focus on molecular imaging.

Aim 2: A graded approach, extending from basic studies to those with an obvious pathway to clinical translation by providing the following specific aims, which focus on high-field magnetic resonance (MR) (Aim 2) imaging.

Title: Molecular Imaging for Macrophage-Associated Pulmonary Inflammation

Time commitments: 1.2 calendar months

Supporting Agency: NIH/NHLBI R01HL116316

Grants Contact: Kimberly Stanton, (301) 435-0519, E-Mail stantonk@nhlbi.nih.gov

PI: Sanjay Jain

Performance Period 9/25/2012- 6/30/2015

Level of Funding: \$245,000

Role: Co-Investigator

Description of Goals: The overall goal is to have a fully validated probe ready for human administration and to file a FDA Investigational New Drug (IND) application at the end of the funding period.

Aim 1: To evaluate [¹²⁵I]DPA-713-SPECT/ PET as a biomarker for serial monitoring of macrophage associated pulmonary inflammation.

Aim 2: To perform cGMP synthesis and toxicology studies for iodo-DPA-713.

Aim 3: To quantify and correlate lesion-specific, multi-modality image parameters across different time-points using in-house computer-assisted image analysis tools.

Title: 177-L.u.n.c.a.

Time commitments 0.24

Supporting Agency: Morphotek Inc. (NCE)

Grants Contact: TBD

PI: Pomper

Performance Period: 8/29/2013-2/28/2015

Level of Funding: \$31,866

Description of Goals: The purpose of this work is to radiolabel the tumor localizing peptide TM801 with the radiometal 177Lu.

Aim 1: 50 mg of TM801+DOTA conjugate will be synthesized (we want enough for several radiolabeling experiments)

Aim 2: 800 microCi of TM801+DOTA+177Lu will be radiolabeled per radiolabeling step
Aim 3: On the order of 700 Ci/mmol of the TM801+DOTA+177Lu conjugate upon radiolabeling

Title: TK-based Infection Imaging

Time Commitments: 1.09

Supporting Agency: NIH, NIBIB R01EB009367 (NCE)

Grants Contact: Florence Turska (301) 496-9314 E-Mail:ft7p@nih.gov

PI: Martin Pomper

Role: Co-Investigator

Performance Period: 05/15/10-04/30/15

Level of Funding: \$267,740

Description of Goals: The goal is to study further musculoskeletal infection, comparing a newly developed method in infection imaging to the current clinical standard of tagged white blood cell (WBC) and attempting to determine the sensitivity and specificity of our technique.

Aim #1: Estimate the sensitivity and specificity of FIAU-PET in detecting orthopedic infection.

Aim #2: To extend the FIAU imaging technique to pulmonary infection.

Aim #3: To transition from [124I]FIAU to [18F]FIAU for imaging bacterial infection.

- **What other organizations were involved as partners?**
 - Nothing to report